

# Annotated Bibliography of Some Papers on Combining Significances or $p$ -values

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## Abstract

A question that comes up repeatedly is how to combine the results of two experiments if all that is known is that one experiment had a  $n$ -sigma effect and another experiment had a  $m$ -sigma effect. This question is not well-posed: depending on what additional assumptions are made, the preferred answer is different. The note lists some of the more prominent papers on the topic, with some brief comments and excerpts.

## 1 Introduction

Suppose one experiment sees a 3-sigma effect and another experiment sees a 4-sigma effect. What is the combined significance? Equivalently, given two  $p$ -values, how can one combine them into one? Since the question is ill-posed (i.e., more information is needed in order to specify the best answer), the statistics literature contains many papers on the topic; a number of them are by prominent statisticians, including in the 1930's Ronald Fisher and both Karl and Egon Pearson. As the existence of this literature may not be well-known, I have put together this bibliography with some introductory comments and some brief descriptions and excerpts. It should be clear that while these general-purpose methods are useful for quick estimates (in particular if estimates of relative weights are available), it is preferable to use additional primary data when available and to take care to understand the nature of the alternative hypotheses.

Given a statistic (function of the data)  $x$ , with (normalized) probability density function  $P(x)$  in the domain  $a < x < b$ , it is common in statistics to introduce the *probability integral transform*, letting

$$y = \int_a^x P(x') dx'. \quad (1)$$

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Then the pdf for  $y$  is uniform on  $(0,1)$ , and without loss of generality many questions about  $x$  can be studied in a more transparent way by considering  $y$ . (If  $x$  is discrete, there are complications which are discussed in some of the cited papers.) Since  $1-y$  is also uniform on  $(0,1)$ , typically some other consideration (such as the distribution of  $x$  under a different  $P$ ) dictates if one end of the interval is of more interest than the other.

If  $x$  is a test statistic and  $P(x)$  its pdf under the null hypothesis  $H_0$ , then for one-sided tests of  $H_0$  at least a vague notion of an alternative hypothesis is needed to specify whether values of  $y$  close to 0 or close to 1 should be considered as evidence against  $H_0$ . Then one can identify either  $y$  (in the former case) or  $1-y$  (in the latter case) with the  $p$ -value, i.e., the smallest value of the significance level  $\alpha$  in Neyman-Pearson hypothesis testing for which  $H_0$  would be rejected. (See [Stuart et al., 1999] for an introduction.) Here I do not address the subtleties of Fisherian vs. Neyman-Pearson interpretation of  $p$ -values, or issues of the utility of  $p$ -values; I merely remind the reader that at best, a  $p$ -value conveys the probability under  $H_0$  of obtaining a value of the test statistic at least as extreme as that observed, and that it should not be interpreted as the probability that  $H_0$  is true.

Frequently the  $p$ -value is communicated by specifying the corresponding number of standard deviations in a one-tailed test of a Gaussian (normal) variate; i.e., one communicates a  $Z$ -value (often called  $S$  in high energy physics) given by

$$Z = \Phi^{-1}(1 - p) = -\Phi^{-1}(p) \quad (2)$$

where

$$\Phi(Z) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^Z \exp(-t^2/2) dt = \frac{1 + \operatorname{erf}(Z/\sqrt{2})}{2}, \quad (3)$$

so that

$$Z = \sqrt{2} \operatorname{erf}^{-1}(1 - 2p). \quad (4)$$

For example,  $Z = 5$  corresponds to a  $p$ -value of  $2.87 \times 10^{-7}$ .

Thus, the question may be asked equivalently as how to combine either a set of  $p$ -values or a set of  $Z$ -values. While the literature addresses the problem in both metrics, most of the detailed studies use the  $p$ -value, where the two-dimensional version (combining  $p_1$  and  $p_2$ ) can be illustrated so transparently: under  $H_0$ , a scatter plot of  $p_2$  vs  $p_1$  uniformly populates the unit square  $(0,1) \otimes (0,1)$ , and one desires a function  $p(p_1, p_2)$  which is uniform on  $(0,1)$ . Contours of  $p$  can be drawn in the  $(p_1, p_2)$  square to illustrate each method of combination.

For combining two  $p$ -values, a general way to construct a combination method is to first choose some function  $f(p_1, p_2)$  which has some perceived desired properties; then calculate the pdf for  $f$  given that  $p_1$  and  $p_2$  are uniform on  $(0,1)$ ; and then transform  $f$  to a  $p$ -value using Eqn. 1 with  $f$  substituting for  $x$ . In some cases, the function  $f$  is by construction already uniform on  $(0,1)$ , so that last step is unnecessary. As for desirable properties of  $f$ , the question is so ill-posed that the only property which is completely general is that of monotonicity, discussed below. For example, in the *complete* absence of additional information  $f(p_1, p_2) = f(p_2, p_1)$  would seem to be desirable. However, even in cases where the details of the combined experiments

are not known, one often knows something about the sample sizes (or more specific information about the precision of the two experiments), in which case there is strong motivation to weight the two  $p$ -values differently.

The ill-posed nature of the problem can be further illustrated by considering the data of two experiments separately and together. For example, suppose two introductory students each make measurements of current vs. voltage across a resistor in order to test the hypothesis that  $I = V/R$ , where  $R$  is given and fixed. For illustration, imagine that all the uncertainty, with normal distribution, is in the current measurement; that the students make  $N_1$  and  $N_2$  measurements, respectively; and that each student then does a chi-square goodness-of-fit test with d.o.f.'s  $N_1$  and  $N_2$ , respectively, and computes the  $p$ -values (from the probability integral transform of the chi-square pdf), with results  $p_1$  and  $p_2$ , respectively. (What is the best goodness-of-fit test is also ill-posed, but that is another, albeit related, story.) Alternatively, the data could be pooled and a chi-square goodness-of-fit test performed with  $N_1 + N_2$  d.o.f., and a  $p$ -value calculated.

In this example, if one has access not to all the data, but only to the four quantities  $p_1$ ,  $p_2$ ,  $N_1$ , and  $N_2$ , then the algorithm for combine the  $p$ -values to obtain the pooled answer is clear: use the inverse of the integral of the chi-square distribution with  $N_1$  and  $N_2$  d.o.f.'s to recover the two student's chi-squares, add them, and then use the chisquare integral with  $N_1 + N_2$  d.o.f. to obtain  $p$ . As with many other algorithms motivated by a specific example, this algorithm is on the list of general-purpose algorithms which can be studied in other problems, in which  $N_1$  and  $N_2$  may be more artificially chosen to give desired weighting to  $p_1$  and  $p_2$ . For this algorithm, the original source commonly cited is [Lancaster, 1961].

One can also readily see that if nuisance parameters are added, complications immediately arise. Thus if  $H_0$  is not  $I = V/R$  with  $R$  *given*, but rather  $I = V/R$  where the student is free to fit for  $R$ , then immediately we see that d.o.f.'s change and more information (in particular the best-fit values of  $R$  and their uncertainties) is needed to recover the pooled  $p$  (which is still possible since the uncertainties carry the information of how the two chi-squares increase as the two fitted values of  $R$  are constrained to an overall best-fit value).

In fact, Lancaster's 1961 method seems to be one of the last general methods to appear in the literature (and was clearly anticipated), the others having appeared in the preceding 30 years. Methods commonly considered, and names usually associated with them, define the combined  $p$  as follows (for  $i = 1, N$ ).

(1) Fisher's method based on the intuitive choice of  $f = \prod p_i$ . As the excerpt from his paper below describes, a simple way to calculate  $p$  uses the relation

$$-2 \sum \ln p_i = \chi_{2N,p}^2, \quad (5)$$

where  $\chi_{\nu,p}^2$  denotes the upper  $p$  point of the probability integral of a central chi-squared of  $\nu$  degrees of freedom.

(2) Good's generalization of Fisher's method to include weights  $\lambda_i$  so that the test

statistic is  $Q = \prod p_i^{\lambda_i}$ , with

$$p = \sum_j \Lambda_j Q^{1/\lambda_j}, \quad \Lambda_j = \lambda_j^{N-1} \prod_{i \neq j} \frac{1}{(\lambda_j - \lambda_i)}. \quad (6)$$

(3) Lancaster's generalization of Fisher's method by adding  $\chi^2$  for dof  $\neq 2$

$$\sum_i (\chi_{\nu_i, p_i}^2)^{-1} = \chi_{\nu_{\text{sum}}, p}^2; \quad \nu_{\text{sum}} = \sum_i \nu_i. \quad (7)$$

(4) Tippett's method using the smallest  $p_i$

$$p = 1 - (1 - (\min\{p_i\}))^N. \quad (8)$$

(5) Wilkinson's generalization of Tippett's method, using the  $k$ th smallest of the  $N$  values of  $p_i$ .

(6) Stouffer's method adding the inverse normal of the  $p_i$ 's,

$$\sum \Phi^{-1}(p_i) = \sqrt{N} \Phi^{-1}(p); \quad i.e., \quad Z = \frac{\sum Z_i}{\sqrt{N}}. \quad (9)$$

(7) Generalization of Stouffer's method to include weights  $w_i$ , by Mosteller and Bush and others,

$$Z = \frac{\sum w_i Z_i}{\sqrt{\sum w_i^2}}. \quad (10)$$

(8) Lipták's even more generalized formula with weights which includes several of the above as special cases: define  $Q$  by substituting a function  $\Psi$  for the normal distribution function  $\Phi$  in Eqn. 2, and proceeding as in the weighted combination of  $Z_i$ 's, calculating the distribution of the result and converting to a  $p$ -value.

It should be clear that *any method for combining  $p$ -values can be used for combining  $Z$  values, and vice versa*. E.g., given any two  $Z$ -values  $Z_1$  and  $Z_2$  (normal variates), a combined  $Z$ -value, also a normal variant, can be constructed from Eqn. 2 where  $p = p(p_1, p_2)$  is obtained by using any  $p$ -value combination method to combine  $p_1 = 1 - \Phi(Z_1)$  and  $p_2 = 1 - \Phi(Z_2)$ .

That this list has grown so long is a testament to the fact that the question is ill-posed! When methods differ significantly, say in combining two  $p$ -values  $p_1$  and  $p_2$ , the difference is typically in how they rank the combination of two similar  $p$ -values compared to the combination of a high one and a low one. Which ranking is preferred depends of course on which parts of the unit square (nearer the axes or nearer the center) the alternative hypotheses tend to populate.

The remainder of this note mentions a number of papers. Section 2 lists notable primary papers. Section 3 lists several reviews which compare some of the above methods. Section 4 list some papers with applications in the life, physical, and social sciences. In most cases, I retain the original author's notation, which corresponds to the above in a transparent way. Most of the papers are readily available on the web, in particular at [www.jstor.org](http://www.jstor.org), which however requires an institutional license.

## 2 Notable Primary Sources

Sir Ronald Fisher’s book, *Statistical Methods for Research Workers*, first appeared in 1925 and has been enormously influential through its many editions. As cited by Karl Pearson [Pearson, 1933], the method for combining significance levels appears to have been introduced in the 4th edition of 1932. The 14th Edition of 1970 reads [Fisher, 1970],

“When a number of quite independent tests of significance have been made, it sometimes happens that although few or none can be claimed individually as significant, yet the aggregate gives an impression that the probabilities are on the whole lower than would often have been obtained by chance. It is sometimes desired, taking account only of these probabilities, and not of the detailed composition of the data from which they are derived, which may be of very different kinds, to obtain a single test of the significance of the aggregate, based on the product of the probabilities individually observed.

“The circumstance that the sum of a number of values of  $\chi^2$  is itself distributed in the  $\chi^2$  distribution with the appropriate number of degrees of freedom, may be made the basis of such a test. For in the particular case when  $n = 2$ , the natural logarithm of the probability is equal to  $-\frac{1}{2}\chi^2$ . If therefore we take the natural logarithm of a probability, change it sign and double it, we have the equivalent value of  $\chi^2$  for 2 degrees of freedom. Any number of such values may be added together, to give a composite test...”

As emphasized by several authors, Fisher’s principle for combining  $p$ ’s is the last line of the first paragraph quoted; the second paragraph is a technical implementation equivalent to performing the probability integral transformation of the product.

Karl Pearson [Pearson, 1933] independently proposed the same test and a variant using  $1 - p$  instead of  $p$ , the latter of which is sometimes called Pearson’s method even though most of his paper is on the same method as Fisher, with more voluminous discussion. He says in a “Note added” that, “After this paper had been set up Dr Egon S. Pearson drew my attention to ... R.A. Fisher’s ...”. (Egon, the Pearson of Neyman-Pearson Lemma fame, was the son of Karl, the Pearson of Pearson’s chi-square.)

E.S. Pearson [Pearson, 1938] briefly reviews the probability integral transformation, “which seems likely to be one of the most fruitful conceptions introduced into statistical theory in the last few years”, and looks at examples of the early methods. He notes the “difference in character” between common alternative hypotheses (goodness of fit problem) and that of different alternative hypotheses for each of the  $p$ ’s. Later he [Pearson, 1950] considered extensions to discrete distributions such as binomial and Poisson.

Tippett [Tippett, 1931] was apparently the first to suggest rejecting  $H_0$  at significance level  $\alpha$  when *any* of  $p_1, \dots, p_k$  is less than or equal to  $1 - (1 - \alpha)^{1/k}$ . I.e., one uses only the smallest  $p$  and corrects for the effect of having  $k$  tries to attain it. Tippett’s method was generalized in a short note by Wilkinson [Wilkinson, 1951] to the case where one observes  $n$  or more significant statistics in a set of  $N$ .

In a landmark sociological study using data from exit interviews of American

soldiers, Stouffer et al. [Stouffer et al., 1949] specified the method which became known as “Stouffer’s method” in an obscure footnote (!), adding three  $Z$ -values (obtained from a Gaussian approximation to binomial data) and dividing by  $\sqrt{3}$ . (The question was whether men with a better attitude had a better chance of promotion, and a positive effect at significance level 5% was found.)

Birnbaum [Birnbaum, 1954] evaluated several methods (Fisher, Pearson, Tippett, Wilkinson) in terms of generally desirable properties such as monotonicity and admissibility. “A test is admissible if there is no other test with the same significance level which, without ever being less sensitive to possible alternative hypotheses, is more sensitive to at least one alternative.” He states “Condition 1: If  $H_0$  is rejected for any given set of  $u_i$ ’s, then it will also be rejected for all sets of  $u_i^*$ ’s such that  $u_i^* \leq u_i$  for each  $i$ .” Then, “...the question is whether any further reasonable criterion can be imposed to narrow still further the class of methods from which we must choose. The answer is no...”. “These considerations prove that to find useful bases for choosing methods of combination, we must consider further the particular kinds of tests to be combined...”. For most of the problems he considers, “Fisher’s method appears to have somewhat more uniform sensitivity to the alternatives of interest...”. Birnbaum also emphasizes that the alternative hypothesis to  $H_0$  depends on the experimental situation and in particular there are two classes, which he calls  $H_A$ : All of the  $u_i$ ’s have the same (unknown) non-uniform, non-increasing density  $g(u)$ ; and  $H_B$ : One or more of the  $u_i$ ’s have (unknown) non-uniform, non-increasing densities  $g_i(u_i)$ .

Good [Good, 1955] generalized Fisher’s product-of- $p$ s method in order to accommodate different positive weights for the results to be combined. He inserted the weights as different exponents for each  $p$ -value in the product, and derived the distribution of the resulting test statistic (assuming unequal weights).

Yates [Yates, 1955], in a paper devoted to issues of combining (discrete) data from  $2 \times 2$  tables, begins by saying that the method of maximum likelihood is preferable, but for quick, possibly preliminary tests, combining via tests such as Fisher’s test with  $n = 2$  (which he takes as the usual test without attribution) “may be regarded as adequate”. Under “Variants of the test”, he writes: “The use of values of  $\chi^2$  for 2 d.f. for the combination of probabilities is to a certain extent arbitrary. It has the convenience that the values are easily calculated, and the use of a function of the product of the probabilities has a certain intuitive appeal, but the method would work equally well with other basic numbers of degrees of freedom. If, for instance, the values of  $\chi^2$  for 1 d.f. corresponding to the  $P$ ’s are summed then in the absence of association the sum will be distributed as  $\chi^2$  for  $k$  d.f.”. He also considers the test that appears to be Stouffer’s test in this context, describing the signed, normalized deviations as “...normal deviates with zero mean and unit standard deviation, and their sum is therefore a normal deviate with a standard deviation of  $\sqrt{k}$ ”, citing as an example Cochran [Cochran, 1954]. ([Cochran, 1954] says that the test criterion,  $\sum X/\sqrt{g}$  using standard normal tables “has much to commend it if the total  $N$ ’s of the individual tables do not differ greatly (say by more than a ratio of 2 to 1) and if the  $p$ ’s are all in the range 20%-80%.”) After considering these variants applied to some examples, Yates does not see much difference and recommends Fisher’s test “on historical grounds and because of its simplicity and intuitive appeal” if one is given

$p$ -values, but Cochran’s combination if one is given the unit variates (as he sees little point in transforming them, as these are only quick approximate calculations). He summarizes unenthusiastically: “Reasons are given for believing that combination of probabilities tests are not likely to be very efficient...”.

In 1958, Lipták [Lipták, 1958] published a very useful overview, unifying and generalizing the theory of the various methods on the market, and elucidating the criteria for a method to be admissible. (Some of this is similar to Birnbaum’s work, of which Lipták seems to have been unaware.) Lipták’s paper, published in a Hungarian journal, unfortunately was overlooked by some subsequent authors, and even today is not available online. He defines the combination problem as that in which “either the null-hypothesis is true in each experiment or the alternative one is valid in each case”. He introduces an “averaging” function  $\chi$ , a strictly increasing and continuous function with domain  $(0,1)$ ; in practice  $\chi$  can be thought of as the *inverse* of the probability integral transformation in Eqn. 1, i.e., it takes a  $p$ -value back to the metric used in some pdf  $P$ . He further introduces weights  $\lambda_i$  for each  $p_i$ ; the combined test statistic is then  $\sum \lambda_i \chi(p_i)$ , the pdf of which can be calculated and transformed to a  $p$ -value using again Eqn. 1 in the forward direction. (Thus his term “averaging function” refers not to the weights, but rather to the function of  $p$  which is to be averaged.) Lipták restricted his paper to the case where the  $\chi$ ’s are all the same (unlike Lancaster). The ill-posed nature of the combination problem is apparent, since (with reasonable assumptions) he shows that for every choice of  $\chi$  and weights  $\{\lambda_i\}$ , there exists a hypothesis testing problem (i.e., an alternative hypothesis) for which that choice is the optimal solution (in terms of Type II error probability) of the combination problem. He also shows that his assumptions (in particular monotonicity) are consistent with Bayesian solutions to the combination problem, noting “The importance of this theorem is clear from the fact that the class of all Bayes solutions in a relatively wide and typical class of hypothesis testing problems are ‘complete’, i.e., for every test there can be given a Bayes solution which is at least as good as this test” (citing A. Wald’s book on statistical decision functions). Lipták shows that methods such as those of Fisher and Stouffer correspond to different choices of  $\chi$  and  $\lambda_i$ . As an omnibus test he advocates the weighted version of Stouffer’s test (Eqn. 10), in which the the weights “should be chosen as to express the efficiencies... of the tests used in the individual experiments.” In a common simple case, this leads to  $\lambda_i = \sqrt{n_i}$ , where  $n_i$  is the number of observations in the  $i$ th experiment, as noted by others as well.

As referred to above, in 1961 Lancaster [Lancaster, 1961] (apparently unaware of Lipták’s paper) generalized Fisher’s method: “Let us suppose that  $P_i$  of the  $i$ th experiment is transformed to the scale of  $v_i = \chi^2$  with  $s_i$  degrees of freedom, and let the simple sum be formed,  $V^* = \sum_{i=1}^N v_i$ , then  $V^*$  is  $\chi^2$  with  $\sum s_i$  degrees of freedom.” He then describes how  $V^*$  can be evaluated using asymptotic properties of the  $\chi^2$  distributions (whereas nowadays one can numerically calculate the tail property, as indicated in Eqn. 7). He notes that weights can be introduced as follows “...if the weights of the different experiments are different, the variation in the degrees of freedom... will give weights to the experiments proportional to the square root degrees of freedom...” Remarkably, Lancaster goes on to say, “On the other hand, it will usually be simpler to obtain standardized normal variables and sum them.

Weighting is then easily introduced as multipliers...”, thus describing the method identical to Stouffer’s method with weights (Eqn. 10) while identifying it only with Yates [Yates, 1955]. Lancaster concludes that it does not matter greatly whether one uses Fisher’s method, the method of normal variates, or his own method, while noting that the normal variate method is computationally easier when there are weights. (As a postscript, in 1967 Lancaster wrote, while discussing the various methods in answer to a query [Lancaster, 1967], that Fisher thought it would be improper to generalize the transformation to  $n \neq 2$  dof.)

Oosterhoff [Oosterhoff, 1969] wrote a monograph on the combination of one-sided tests, including a historical introduction, various theorems, and some graphs of acceptance regions. (This followed earlier work by Zwet and Oosterhoff [van Zwet and Oosterhoff, 1967].) Sprott [Sprott, 1971] reviewed the book, describing the “interesting historical survey” but otherwise finding it of narrow interest and that “it would appear to have limited value to a practising statistician involved with practical problems.”

Berk and Cohen [Berk and Cohen, 1979], consider a criterion of optimality known as Bahadur relative efficiency, and categorize methods as asymptotically Bahadur optimal (ABO) or not. Fisher’s method is ABO [Littell and Folks, 1971, Littell and Folks, 1973], but there are many other ABO unweighted methods. [Berk and Cohen, 1979] is particularly interesting because it considers weighted methods as well. It concludes that Lancaster’s method [Lancaster, 1961] is ABO but Good’s method [Good, 1955] is not. They describe Lancaster’s method in terms of the  $\Gamma$  function rather than the related chi-square distribution, defining  $W_i = \{\Gamma_{\alpha_i}^{-1}(1 - L(T_i, n_i))\}/n$ , where  $\Gamma_{\alpha_i}$  is the gamma cumulative distribution function, with parameters  $\alpha_i$  and  $\frac{1}{2}$ . (The  $L$ ’s are the  $p$ -values.) “There is complete flexibility in the choice of the  $\alpha_i$ ’s, which play the role of weights ... The statistic  $W_\Gamma = \sum W_i$  is such that  $nW_\Gamma$  has a  $\Gamma(\sum \alpha_i, \frac{1}{2})$  distribution, so that critical values are readily attainable from chi-squared tables if  $\sum \alpha_i$  is an integer.”

Wright [Wright, 1992] discusses, with numerous references, the problem of adjusting the  $p$ -value of an individual test, when taken in the context of other tests. While this seems to be closely related to the problem of combining  $p$ -values, the literature appears to be disjoint from that in the rest of this bibliography, and I have not pursued it.

For combining tests of correlation coefficients, Han [Han, 1989] proposed a test based on a weighted linear combination of Fisher  $z$  transformations of the  $p$ -value. N.I. Fisher [Fisher, N. I. et al., 1990] commented that the Lancaster [Lancaster, 1961] generalization of Fisher’s test was of interest to try as well, and in the reply to comment, Han says that Lancaster’s method was better than the unweighted Fisher test, but had smaller power than Han’s test in most cases.

For the special case of “balanced incomplete block design” Mathew et al. [Mathew et al., 1993] describe a combination procedure which they say outperforms Fisher’s method (which they suggest is likely to be inadmissible). They also emphasize the distinction between common and separate alternative hypotheses.

Goutis et al. [Goutis et al., 1996] attempt to state formally their “axioms” which a  $p$ -value combination scheme should satisfy, based partially on comparison with a



Bayesian model. They cite [Birnbaum, 1954] but make the point that decision theory may not be a reliable guide. The discussion points to the need for more information about the experiments than just the  $p$ -values, noting that combining combinations of  $p$ -values is problematic. “We can say that evidential measures based on combining rules of Fisher and Tippett seem to perform reasonably...”. Regarding the decision theoretic approach and their axiomatic approach, “...we are unable to reconcile the two approaches...”.

### 3 Reviews

In comparing methods, reviews necessarily consider some classes of alternatives to  $H_0$ , and hence the conclusions can vary, or even contradict each other, depending on the alternatives chosen.

Rosenthal [Rosenthal, 1978] surveys nine methods used in psychology, and says that “the seminal work of Mosteller and Bush [Mosteller and Bush, 1954] is especially recommended”. He finds limitations with the Fisher method, and concludes: “There is no best method under all conditions [Birnbaum, 1954], but the one that seems most serviceable under the largest range of conditions is the method of adding  $Z$ s, with or without weighting” (i.e., Stouffer’s method, with or without modification by Mosteller and Bush).

The same year, Koziol and Perlman [Koziol and Perlman, 1978] considered the non-central chi-square problem, including the sum of chi-squares statistic with different d.o.f., emphasizing that different combination methods have advantages depending on the alternative hypothesis. One of their conclusions was, “It is difficult to recommend the inverse normal procedure in any circumstance”. This is remarkable in view of Rosenthal’s conclusion and the apparent popularity of Stouffer’s method in psychology.

Loughin [Loughin, 2004] studies six methods. He cites Lipták [Lipták, 1958] for the unweighted  $z$  method instead of the more usual Stouffer citation, and cites Mosteller and Bush only to say that he (Loughin) does not consider weights in this paper. He has some nice comparisons in the unit square, and notes that all the methods considered satisfy a property of *monotonicity*: “rejecting  $H_0$  for  $\{p_1, \dots, p_k\}$  implies rejecting  $H_0$  for all  $\{p_1^*, \dots, p_k^*\}$  such that  $p_i^* \leq p_i$ ,  $i = 1, \dots, k$ . Holding everything else constant, greater evidence against  $H_{0i}$  implies greater evidence against  $H_0$ .”

Marden, in two papers which begin with a brief review, studies the performance of many of the above tests when applied to non-central chi-squared tests or  $F$  tests [Marden, 1982]; and non-central  $t$  or normal mean tests [Marden, 1985]. The inverse normal procedure (Stouffer’s test) is found to be inadmissible in both papers.

In their book on of meta-analysis (the modern term for combining results from different experiments or trials), Hedges and Olkin [Hedges and Olkin, 1985] devote Chapter 3 to methods for combining tests, reviewing all of the methods described above. They conclude, “It seems that Fisher’s test is perhaps the best one to use if there is no indication of particular alternatives”.

## 4 Some papers with Applications and Discussion

In high energy physics (HEP), the first and second editions of the popular text [Eadie et al., 1971], [James, 2006] describe Fisher’s method. Cousins [Cousins, 1994] discusses Fisher’s method and generalizations to  $n \neq 2$ , in particular to  $n = 1$  by G. Irwin, but was apparently aware of neither [Lancaster, 1961] nor Fisher’s insistence [Lancaster, 1967] on  $n = 2$  due to the product-of- $p$ -values derivation. Recently in HEP, Bitjukov et al. [Bitjukov et al., 2006] advocate a method which is essentially Stouffer’s method (without the generalization [Mosteller and Bush, 1954], [Lipták, 1958] [Lancaster, 1961] to include weights).

In a more substantive HEP paper, Janot and Le Diberder [Janot and Le Diberder, 1998] discuss various optimality and reasonableness considerations and propose a method with a weighted combination scheme which can be identified as that of Good [Good, 1955]. (The formula for the combined  $p$ -value (Eqn. 6 above) is their Eqn. (38) and Eqn. (1) of [Good, 1955].) They discuss in detail the choice of optimal weights, as well as extensions to the discrete case, in particular low-statistics Poisson variates encountered in frontier HEP experiments, with consideration of reducible and irreducible background.

In astrophysics, Afonso et al. [Afonso et al., 2003] use Lipták’s [Lipták, 1958] weighted generalization of Stouffer’s method in a search for gravitational lensing events, using as weights the expected number of events of each experiment for each lens mass.

In evolutionary biology, Whitlock [Whitlock, 2005] compares Fisher’s method and the weighted Stouffer method of Mosteller and Bush [Mosteller and Bush, 1954], and concludes that the latter is better; this is perhaps not surprising since it uses additional information. He notes that Stouffer’s method was originally “given in a footnote on p. 45 of their sociological work on the Army . . . This must be one of the most obscure origins of a statistical method in the literature”.

Zaykin et al. [Zaykin et al., 2002], in gene studies, review possibilities and advocate a variant of Fisher’s method in which only  $p$ -values below some truncation value are used. Among the advantages, they state, “Experience shows that the ordinary Fisher product test loses power in cases where there are a few large  $p$ -values.” They study power in cases relevant for them. Neuhauser and Bretz [Neuhauser and Bretz, 2005] do some studies of the truncation.

In molecular biology, Koziol [Koziol, 1996] explores the relationship between the weighted methods of Good [Good, 1955] and Lipták [Lipták, 1958]. Koziol and Tuckwell [Koziol and Tuckwell, 1999] consider as well these tests from a Bayesian point of view. “Fisher’s well-known combination procedure. . . is found to be a Bayes test in this setting with a noninformative prior. Good’s weighted version of Fisher’s procedure is shown to be an excellent approximation to other Bayes tests.”

Psychology professors Darlington and Hayes [Darlington and Hayes, 2000] consider the Stouffer  $z$  method to be the best-known method, and propose extensions to it and other methods. They note, “As a general rule, the Stouffer method yields a numerically smaller (thus, more significant) pooled  $p$  than the Fisher method if the entering  $p$ s are fairly similar in value, whereas that Fisher method yields a more

significant result if the entering  $ps$  vary widely.” They advocate the method they call Stouffer-max, which considers only the  $s$  most significant results (out of  $k$ ).

In economics, Wallis [Wallis, 1942] discusses Fisher’s solution, emphasizing forcefully the derivation based on product of probabilities, lamenting that it is misunderstood that  $\chi^2$  with  $n = 2$  was chosen for convenience: “This reasoning is entirely fallacious. . . that transformation, when used, is valid only for two degrees of freedom.” But having said that, he proceeds to investigate if the product of the probabilities is indeed the proper criterion of joint significance, and does so using the Neyman-Pearson Lemma for comparison. He concludes the Fisher’s test probably excludes a region “not radically different from the ideal region” in the kind of problems “most likely to be found practical work”. He goes on to consider the discrete case. As another indication of the galaxy of people who have thought about this problem, it is interesting that Wallis is “indebted to Milton Friedman for collaborating in the investigations” of one section of the paper and for “many stimulating discussions”.

Louv and Littell [Louv and Littell, 1986] compare six of the usual methods in the case of tests on a binomial parameter, with detailed discussion of the circumstances in which each has advantages or disadvantages, also making the distinction of whether or not the alternative is common to all  $p_i$ ’s.

Westberg [Westberg, 1985] compares Fisher’s method and Tippett’s method, and discusses when she recommends each. “The selection of a combination procedure is difficult. You should consider which is the most interesting deviation from  $H_0$  if the null hypothesis is not true, and also the number of interesting hypotheses that are false.” “Bahadur’s efficiency is an asymptotic concept . . . the asymptotic result does not actually carry over to finite samples.”

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